HIV/AIDS

Trends in HIV testing, serial HIV prevalence and HIV incidence among people attending a Center for AIDS Prevention from 1988 to 2003

I Hurtado, I Alastrue, I Ferreros, J del Amo, C Santos, T Tasa, I Hernández-Aguado, S Pérez-Hoyos

Sex Transm Infect 2007;**83**:23–28. doi: 10.1136/sti.2005.019299

See end of article for authors' affiliations

Correspondence to: Mrs Hurtado, Unitat d'Epidemiologia i Estadística, Escola Valenciana d'Estudis en Salut (EVES), C/Juan de Garay 21, 46017 Valencia, Spain; hurtado_isa@gva.es

Accepted 16 May 2006
Published Online First 6 June 2006

Aim: To analyse trends in HIV testing, serial HIV prevalence and HIV incidence among people who underwent voluntary testing in a Center for AIDS Prevention in Valencia, Spain.
Methods: Open cohort study including all subjects who went to the Center for AIDS Prevention from 1988 to 2003. Information on sociodemographic variables and HIV test results was collected. Serial prevalence and incidence rates were calculated, and joinpoint regression was used to identify changes in trends over time.
Results: 21 241 subjects were analysed; 67% men, 27% injecting drug users (IDUs), 43% heterosexuals and 13% men who have sex with men (MSM). From 1988 to 1990, IDUs accounted for 57% of clinic attenders, decreasing to 14% by 1997–2003, accompanied by an increase in heterosexuals. Overall, HIV prevalence for the whole period was 15%, dropping from 35% to <10% after 1999 and to 3% by 2003, when HIV prevalence was 26% in IDUs, 6% in MSM and 2% in heterosexuals. Total HIV incidence was 2.5%. From 1988 to 1990, HIV incidence ranged from 6% to 8%, and a gradual and progressive decline observed from 1990 onwards. From 1995 onwards, HIV incidence was <2%. The highest incidence rate is seen in IDUs, 7–12% in the first period and 4–5% at the end. Among MSM, a change in the decreasing trend is seen by 1998, and increases in incidence are detected by 2002–3.
Conclusions: Serial HIV prevalence has markedly decreased from 1988 in all transmission categories, although it is still high. With regard to HIV incidence, the drop has been marked too, although a worrying increase, that requires further follow-up, has been detected in MSM in the past 2 years.

From its start in the 1980s, the HIV epidemic has become one of the most relevant public health problems worldwide. In Spain, the epidemic has been characterised by large numbers of HIV infected injected drugs users (IDUs), although over the past few years the proportion of people infected through sexual transmission seems to be steadily increasing. However, little data are available on HIV infection trends over time.

Similar to what had been reported in other industrialised countries, the introduction of the highly active antiretroviral treatment (HAART) in 1996 dramatically reduced the incidence of AIDS and AIDS-associated mortality in Spain.[1 2] This decline, however, ceased by the year 2000, and a rebound in the number of AIDS cases in men who have sex with men (MSM) was noticed.[3] AIDS registers have ceased to be adequate tools for HIV surveillance since 1996, calling for the need to implement appropriate systems to monitor HIV infection. Population-based HIV registers are progressively becoming the best tool in HIV surveillance in Europe, although in Spain, only 3 of the 17 autonomous regions have implemented a double information system with data from both HIV infections and AIDS cases. The three available HIV registers in Spain also show a steady increase in the proportion of HIV infections acquired through sexual transmission. Nevertheless, one of the best ways to monitor the evolution of HIV infection is the measurement of HIV incidence and serial prevalence of new HIV infections among people with high-risk behaviours in well-characterised cohorts over long periods of time.

In western Europe, diagnoses of HIV among people infected through heterosexual contact increased between 1997 and 2002.[4] This increase was also observed among MSM, a trend that reversed the slow decrease observed during the preceding years.[5] Indeed, studies carried out in San Francisco, Amsterdam and London[6 7] identified increases in new HIV infections in MSM, together with increases in rectal gonorrhoea and syphilis outbreaks in the context of the HAART euphoria, which lead to relaxation of safe sex practices. In Spain, only Del Romero *et al*[8] have described an increase in HIV incidence in 2001 among MSM in Madrid.

The Centers for AIDS Information and Prevention (CIPS) were created in 1987 as open-access clinics to offer free and confidential HIV testing and counselling. This allowed the establishment of an information system, which enabled serial HIV test results to be obtained.[9 10] The aim of this study was to analyse trends in HIV testing, serial HIV prevalence and HIV incidence among people who underwent voluntary testing in a CIPS in Valencia, Spain, from 1988 to 2003.

SUBJECTS AND METHODS

This study has been carried out in a CIPS in Valencia, whose objective is to provide HIV information and counselling, free and anonymous HIV testing as well as testing for hepatitis B virus, hepatitis C virus, hepatitis A virus and syphilis. An open cohort study was established to include all subjects who went to this centre for voluntary HIV testing from 1988 to 2003. More information about the cohort can be obtained elsewhere.[9] A soundex code constructed with the date of birth, sex, name and surname initials was used to anonymously identify the individual and link the subjects' tests. Before HIV testing, a personal face-to-face interview was carried out by health professionals where information on different sociodemographic variables and risk practices was collected. Clinic attenders

Abbreviations: IDU, injecting drug user; MSM, men who have sex with men; HAART, highly active antiretroviral treatment; CIPS, Centers for AIDS Information and Prevention

receive pre-test and post-test information and counselling on HIV preventive measures. Subjects are also offered vaccination against hepatitis A virus and hepatitis B virus. Subjects who report HIV transmission risk practices are invited to attend the centre every 6 months. ELISA was used to determine the presence of HIV antibodies, and western blot to confirm positive results.

Transmission categories have been divided into three mutually exclusive groups: IDUs, MSM and heterosexuals. Separate analyses for these categories were carried out.

Statistical analyses

We considered those subjects who tested HIV positive on their first visit to the CIPS to be HIV prevalent. We calculated the HIV prevalence for each year to construct the serial HIV prevalence for the study period. We considered those subjects who tested HIV negative and had an HIV positive test in a subsequent visit in 3 years from the last negative result to be incident. Only negative tests carried out at CIPS were considered. Seroconversion was imputed through the midpoint estimate between the last HIV-negative and the first HIV-positive.

A description of the evolution of HIV serial prevalence by transmission category and calendar year was carried out. Also, the annual rates of HIV incidence were calculated, placing identified seroconverters in the numerator, and the person's time at risk for seroconversion (follow-up time of subjects who tested HIV-negative and had further visits to the CIPS) in the denominator. For seroconverters, follow-up time was considered up to the date of estimated seroconversion.

After representing the HIV serial prevalence and incidence rates, a ''joinpoint'' regression model was used to test for marked changes in the trend of the series.[11] A model in logarithmic scale was used (ie, log prevalence = $\beta \times$time) assuming Poisson variation for incidence. The analyses started with a minimum number of changes (eg, none) contrasting the existence of one or more changes (up to 3). After identifying the existence of a change in the trend, a segmented regression was fit and the result of the best model was shown graphically for all subjects and stratified by transmission category. For calculating HIV serial prevalence and incidence, we used the STATA V 8.0 programme, and the Surveillance Research Program of the US National Cancer Institute software[12] for the joinpoint regression.

RESULTS

A total of 21 241 subjects aged >14 years underwent voluntary HIV testing in the CIPS from 1988 to 2003. Of these, 27% (5705) were IDUs, 43% (9221) were heterosexuals and 13% (2831) were MSM. Overall, 67% were men (table 1). A marked increase in the number of people undergoing testing over the study period was observed. Around 600 people visited the CIPS in 1988, increasing to 1500 in 1992. This testing pattern was more or less maintained up to 1999 when the CIPS changed its location, and the number of people undergoing testing per year fell to 1200, increasing to 1300 by 2002–3. During 1988–90, the percentage of IDUs was 57%, decreasing to 14% by 1997–2003. This decrease in the percentage of IDUs was accompanied by an increase in that of heterosexuals, which rose from 18% in 1988–90 to 56% in 1997–2003. The proportion of MSM was relatively stable over time (table 1). Distribution by age has remained more or less constant throughout the 16 years, the largest group being that of 26–35 years, accounting for 47% of the people (table 1).

Overall, 3234 subjects had an HIV positive result, representing an HIV prevalence of 15% for the whole period. From 1988 to 1990, overall HIV prevalence was around 35%, decreasing throughout the years, dropping to <10% after 1999 and further to 3% by 2003 (table 2). Despite the marked decrease in HIV prevalence, IDUs still have a high HIV prevalence (26%, by 2003). The highest HIV prevalence in MSM was observed in 1990 (25%), dropping to <10% by 1999 and to 6% in 2003. In heterosexuals, HIV prevalence was clearly lower during all the periods, being the highest (11%) in 1988 and 1991, and 2% in 2003 (table 2). A decrease in the overall HIV serial prevalence during the period was observed, with a marked change in the trend detected in 1990 (fig 1). No changes in the descending trend were found when stratified analyses were carried out.

Of those subjects who tested HIV negative at first visit, 4424 (21%) came back for another HIV test; 38% among IDUs, 46% among MSM and 22% among heterosexuals. Of those repeat testers, 340 (7.7%) seroconverted during 13 761.184 persons-years of follow-up, yielding an HIV incidence rate of 2.5% (table 3). The highest incidence rate (from 6% to 8%) was observed from 1988 to 1990. A strong decrease in HIV incidence was observed from 1988 to 1995, followed by an attenuated decline from 1995 onwards (fig 2). A marked change in the slope of HIV incidence was observed after 1995, after adjusting a joinpoint regression model. The highest incidence rates were among IDUs and the lowest among heterosexuals (table 3 and fig 2). No changes in trends were detected after adjusting jointpoint regression models for either of these groups.

Among MSM, a decline in HIV incidence rates was observed from the late 1980s onwards, similar to the trends in the other groups. However, a significant change in the trend was detected from 1998 onwards. After adjusting the jointpoint regression model, a significant increase ($p<0.05$) in HIV incidence rates was observed (fig 2).

DISCUSSION

We have shown how serial HIV prevalence in our setting has markedly decreased from 1988 in all transmission categories, although it is still high. This reduction is largely due to two factors: the decrease in the number of IDUs who visit the CIPS and the decrease in HIV prevalence in IDUs, which declined from 50% by 1988–90 to 26% by 2003. With regard to HIV incidence, the drop has been very marked too, although a worrying increase in new HIV infections was detected in MSM in 2002–3.

The number of people attending CIPS over the years has gradually increased. Also, a significant change in the demographic profile of visitors has taken place. The number of IDUs, the group with the highest HIV prevalence, has decreased throughout the years, whereas the number of heterosexuals coming for HIV testing and counselling has increased. These are, in themselves, remarkable findings, as they highlight the changes of the populations that perceive themselves at risk and self-select themselves for HIV testing.

During the period analysed, total HIV serial prevalence decreased drastically since the late 1980s. However, an important testing bias must be taken into account, because immediately after opening the CIPS (the first centres to offer anonymous, free and confidential HIV testing), a large number of undiagnosed HIV-infected people came for testing, resulting in an artificially high initial HIV prevalence. Despite a decrease in HIV prevalence in IDU from the 1980s to early 2000, it is noteworthy that serial HIV prevalence in IDU is still extremely high; indeed, around one in every four IDUs who come for testing is HIV positive. The decrease in HIV prevalence observed is most probably the result of the prevention efforts carried out among drug users, such as harm-reduction interventions, which include methadone administration and needle exchange programmes.[3 13 14] These programmes, together with health promotion campaigns have also led to a reduction in the number of new IDUs in Spain.[3 13 15] Our data, nevertheless, support the need to maintain and reinforce these programmes.

Table 1 Descriptive characteristics of people who underwent voluntary testing in the Center for AIDS Information and Prevention, Valencia, Spain, 1998–2003

	Total (n = 21241)	1988–90 (n = 2927)	1991–96 (n = 9158)	1997–2003 (n = 9156)
Sex				
Male	14196 (67%)	2034 (70%)	6260 (68%)	5902 (65%)
Female	7045 (33%)	893 (30%)	2898 (32%)	3254 (35%)
Age group (years)				
15–25	6970 (33%)	1102 (38%)	3055 (33%)	2813 (31%)
26–35	10000 (47%)	1436 (49%)	4356 (48%)	4208 (46%)
>35	4271 (20%)	389 (13%)	1747 (19%)	2135 (23%)
Transmission category				
IDU	5705 (27%)	1664 (57%)	2777 (30%)	1264 (14%)
MSM	2831 (13%)	279 (10%)	1307 (14%)	1245 (14%)
HT	9221 (43%)	532 (18%)	3570 (39%)	5119 (56%)
Other	3484 (17%)	452 (15%)	1504 (17%)	1528 (16%)

HT, heterosexual; IDU, injecting drug user; MSM, men who have sex with men.

Trends in total HIV incidence over time have been similar to HIV serial prevalence, with a spectacular decrease from high initial levels.[9 16] However, we have detected a worrying increase in HIV incidence in MSM in 2002–3, although caution is needed in the interpretation of this increase and further follow-up will confirm this trend. This increase could reflect either ineffective HIV prevention messages caused by relaxing risk practices or the use of HIV testing by people as a tool to measure risk. Increases in new HIV infections and other sexually transmitted diseases have been described in MSM in the HAART era in large cities in Western countries.[5] In Los Angeles and San Francisco, an increasing number of cases of syphilis and other sexually transmitted infections were reported among MSM in 2000. In western Europe, diagnoses of HIV among MSM increased by 22% during 2001–2,[4] a trend that reverses the slow descent observed during the preceding years. Outbreaks of primary

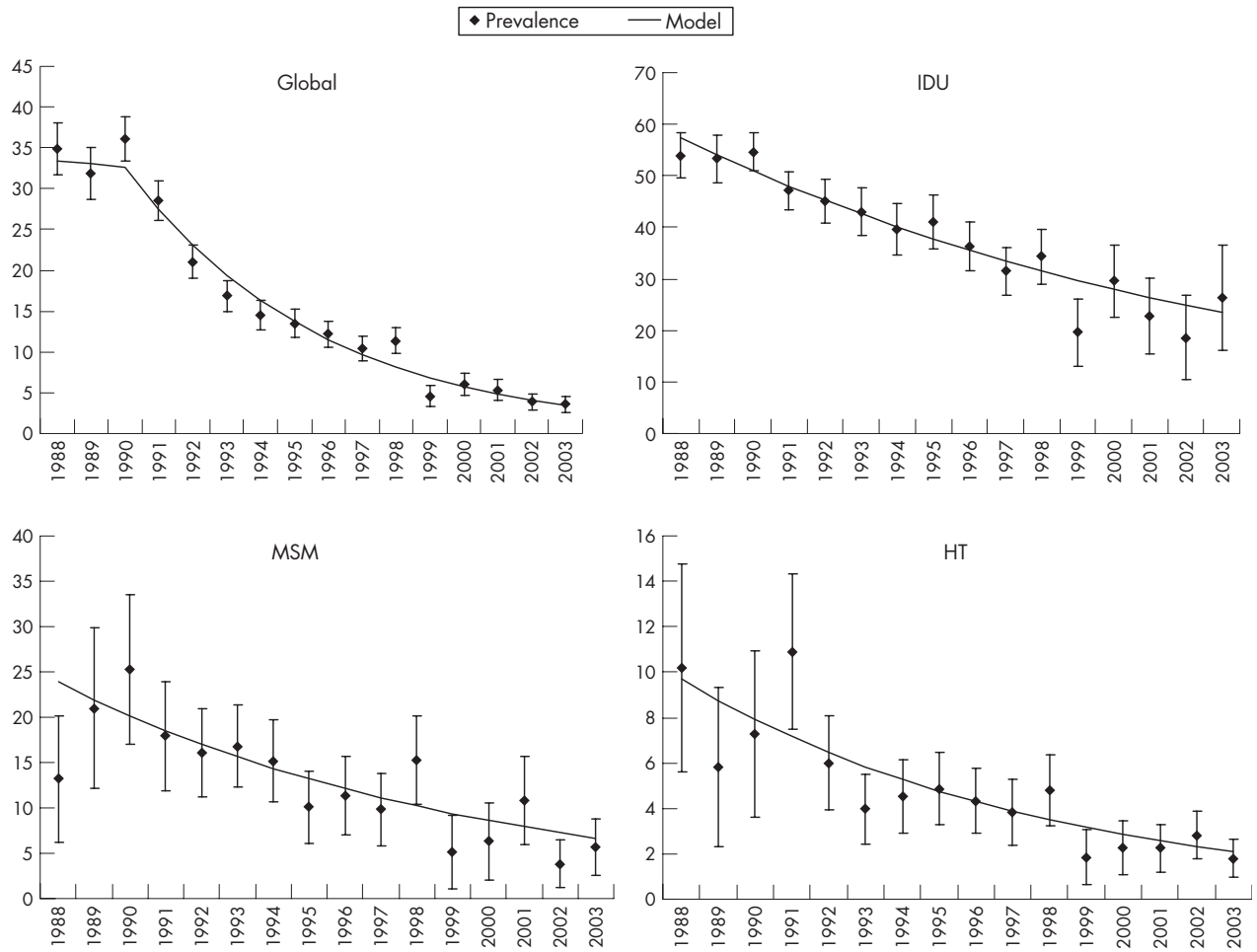

Figure 1 Trends in HIV prevalence by transmission category of people who underwent voluntary testing in the Center for AIDS Information and Prevention, Valencia, Spain, between 1988 and 2003. Jointpoint regression model fitted.

Table 2 HIV serial prevalence by calendar and transmission category of people who underwent voluntary testing in the Center for AIDS Information and Prevention, Valencia, Spain, 1988–2003

	Total*		IDU		MSM		HT	
Year	HIV+	Prevalence (%; 95% CI)	HIV+	Prevalence (%; 95% CI)	VIH+	Prevalence (%; 95% CI)	VIH+	Prevalence (%; 95% CI)
1988	234	34 (30 to 38)	207	52 (47 to 57)	11	16 (7 to 25)	15	11 (6 to 16)
1989	265	32 (29 to 35)	234	53 (48 to 58)	17	21 (12 to 30)	10	6 (2 to 10)
1990	445	36 (33 to 39)	398	55 (51 to 59)	27	25 (17 to 33)	14	7 (3 to 11)
1991	393	28 (26 to 30)	327	47 (43 to 51)	28	18 (12 to 24)	35	11 (8 to 14)
1992	317	21 (19 to 23)	239	45 (41 to 49)	36	16 (11 to 21)	30	6 (4 to 8)
1993	265	17 (15 to 19)	189	43 (38 to 48)	44	17 (12 to 22)	25	4 (2 to 6)
1994	219	14 (12 to 16)	150	4 (35 to 45)	37	15 (11 to 19)	29	4 (2 to 6)
1995	206	13 (11 to 15)	139	41 (36 to 46)	22	10 (6 to 14)	35	5 (3 to 7)
1996	204	12 (10 to 14)	144	36 (31 to 41)	23	11 (7 to 15)	33	4 (3 to 5)
1997	166	1 (9 to 11)	118	31 (26 to 36)	21	10 (6 to 14)	25	4 (2 to 6)
1998	177	11 (9 to 13)	105	34 (29 to 39)	32	15 (10 to 20)	35	5 (3 to 7)
1999‡	46	5 (4 to 6)	28	19 (13 to 25)	6	5 (1 to 9)	9	2 (1 to 3)
2000	69	6 (5–7)	47	29 (22 to 36)	8	6 (2 to 10)	14	2 (1 to 3)
2001	63	5 (4–6)	28	23 (16 to 30)	17	11 (6 to 16)	17	2 (1 to 3)
2002	51	4 (3–5)	16	19 (11 to 27)	8	4 (1 to 7)	26	3 (2 to 4)
2003	48	3 (2–4)	19	26 (16 to 36)	12	6 (3 to 9)	17	2 (1 to 3)

HT, heterosexual; IDU, injecting drug user; MSM, men who have sex with men.
* Includes IDU, MSM, HT and Other categories.
‡This year CIPS remained closed last quarter.

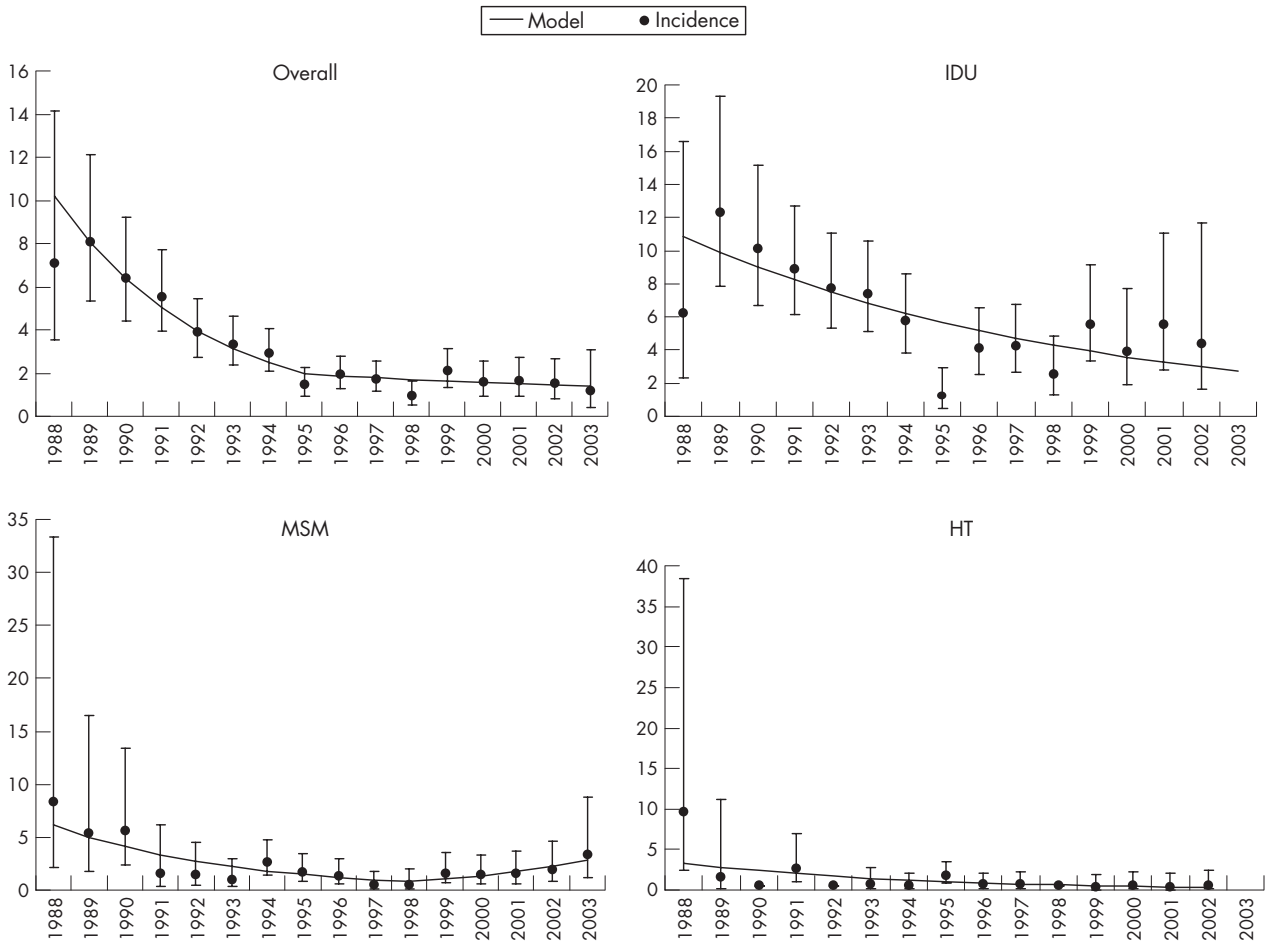

Figure 2 Trends in HIV incidence rates (×100 person-years) by transmission category of people who underwent voluntary testing in the Center for AIDS Information and Prevention, Valencia, Spain, 1988–2003. Jointpoint regression model fitted.

Table 3 HIV incidence by calendar and transmission category of people who underwent voluntary testing in the Center for AIDS Information and Prevention, Valencia, Spain, 1988–2003

	Overall*			IDU			MSM			HT		
Year	n†	Incident cases	Rate×100 per year (95% CI)	n†	Incident cases	Rate×100 per year (95% CI)	n†	Incident cases	Rate×100 per year (95% CI)	n†	Incident cases	Rate×100 per year (95% CI)
1988	226	8	7.06 (3.5 to 14.1)	131	4	6.22 (2.3 to 16.6)	45	2	8.34 (2.1 to 33.3)	43	2	9.59 (2.4 to 38.3)
1989	422	23	8.06 (5.3 to 12.1)	226	19	12.3 (7.8 to 19.3)	86	3	5.33 (1.7 to 16.5)	99	1	1.56 (0.2 to 11.1)
1990	616	28	6.37 (4.4 to 9.2)	335	23	10.07 (6.7 to 15.1)	119	5	5.56 (2.3 to 13.4)	139	0	0.00
1991	879	35	5.52 (4.0 to 7.7)	454	29	8.84 (6.1 to 12.7)	189	2	1.55 (0.4 to 6.2)	206	4	2.61 (1.0 to 6.9)
1992	1121	32	3.85 (2.7 to 5.4)	486	29	7.70 (5.3 to 11.1)	292	3	1.43 (0.4 to 4.4)	309	0	0.00
1993	1294	34	3.31 (2.4 to 4.6)	485	29	7.34 (5.1 to 10.5)	389	3	0.96 (0.3 to 3.0)	384	2	0.70 (0.2 to 2.8)
1994	1499	35	2.91 (2.1 to 4.1)	505	23	5.71 (3.8 to 8.6)	478	10	2.58 (1.4 to 4.8)	472	2	0.55 (0.1 to 2.2)
1995	1618	19	1.46 (0.9 to 2.3)	505	5	1.22 (0.5 to 2.9)	517	7	1.64 (0.8 to 3.4)	531	7	1.69 (0.8 to 3.5)
1996	1709	26	1.91 (1.3 to 2.8)	521	17	4.08 (2.5 to 6.6)	531	6	1.36 (0.6 to 3.0)	588	3	0.69 (0.2 to 2.1)
1997	1720	23	1.70 (1.1 to 2.6)	539	18	4.26 (2.7 to 6.7)	546	2	0.45 (0.1 to 1.8)	560	3	0.71 (0.2 to 2.2)
1998	1567	11	0.90 (0.5 to 1.6)	476	9	2.51 (1.3 to 4.8)	497	2	0.49 (0.1 to 2.0)	521	0	0.00
1999	1279	22	2.06 (1.3 to 3.1)	332	15	5.52 (3.3 to 9.2)	428	6	1.58 (0.7 to 3.5)	456	1	0.28 (0.03 to 2.0)
2000	1216	15	1.54 (0.9 to 2.5)	266	8	3.86 (1.9 to 7.7)	413	5	1.41 (0.6 to 3.4)	472	2	0.57 (0.1 to 2.2)
2001	1163	14	1.60 (0.9 to 2.7)	196	8	5.53 (2.8 to 11.0)	411	5	1.51 (0.6 to 3.6)	497	1	0.29 (0.04 to 2.1)
2002	1052	11	1.48 (0.8 to 2.7)	128	4	4.39 (1.6 to 11.7)	362	5	1.91 (0.8 to 4.6)	502	2	0.59 (0.1 to 2.3)
2003	715	4	1.15 (0.4 to 3.1)	76	0		239	4	3.28 (1.2 to 8.7)	353	0	

HT, heterosexual; IDU, injecting drug user; MSM, men who have sex with men.
* Includes IDU, MSM, HT.
† Number of people at risk.

syphilis were reported in the UK in 2002.[8] In Madrid, increases in HIV incidence were also detected in MSM attending a large HIV/STD clinic in 2000.[8] Among the reasons proposed to explain these data, ''prevention fatigue'' and ''confidence excess'' have been put forward, as a result of the better survival expectations derived from antiretroviral treatments.[4 7] It is essential to enhance programmes dealing with this worrying increase.

The HIV epidemic is affecting new population segments, with a growing proportion of people infected through unprotected heterosexual sex. In western Europe, an increasing trend of new diagnoses of HIV in heterosexuals has been observed, with important proportions occurring among migrants or ethnic minorities.[4] Our data do not support these observations, as decreases in both HIV prevalence and HIV incidence among heterosexuals are observed. Data about country of origin were not available for the whole period, as the arrival of migrants to Spain took place in the late 1990s. Collecting this information began in 2001. These reported trends are probably explained by the changes in the profile of heterosexuals taking up testing in the CIPS, indicating an increase in the risk perception of this group of the population.

This study has some inherent limitations resulting from the selection biases operating in the population volunteering for HIV testing. These figures reflect results from voluntary HIV tests of people with, presumably, risk practices. The testing bias, which could explain the high initial HIV first-time prevalence has already been mentioned. It is important to highlight that the CIPS was a pioneer centre in Valencia, the first to offer free and anonymous voluntary HIV tests, and that until the mid-1990s, most IDUs undergoing drug detoxification went there for HIV testing. From the mid-1990s onwards, as other HIV testing units appeared,[17] this referral pattern became less marked. Despite these changes, the stable structure of the CIPS enables us to infer that the described trends reflect the closest picture of the changes in HIV epidemiology in the population which perceives itself at risk and that takes up voluntary HIV tests in our community.[18]

In summary, we have described important declines in serial HIV prevalence from 1988 to 2003 in all transmission categories. Despite this decrease, high HIV prevalence is still seen in IDUs. More worrying, however, is the apparent increase in HIV incidence observed in MSM in 2002–3, which requires follow-up to confirm trends. It is still essential to link surveillance with preventive actions to reduce HIV transmission in the community.

Authors' affiliations

I Hurtado, I Ferreros, S Pérez-Hoyos, Unitat d'Epidemiologia i Estadística, Escola Valenciana d'Estudis en Salut (EVES),.Valencia, Spain
I Alastrue, C Santos, T Tasa, Centro de Información y Prevención del SIDA de Valencia, Valencia, Spain
J del Amo, I Hernández-Aguado, Dpto Salud Pública, Universidad Miguel Hernández de Alicante, Alicante, Spain

Funding: This work was financed through grants from FIS (Fondo de Investigación Sanitaria; 02/0639) and Becas de la Consellería de Sanitat de la Generalitat Valenciana B12/03 and B15/04.

Competing interests: None.

IH and SP-H designed the study, IH, IF and SP-H carried out the statistical analysis. IA, CS and TT were responsible for the recruitment and data collection. IH-A set up the original study and collaborated in its design. IH, SP-H and JDA wrote and interpreted the results. All the authors revised the different versions of the manuscript.

REFERENCES

1 **Mocroft A**, Ledergerber B, Katlama C, *et al*. Decline in the AIDS and death rates in the EuroSIDA study: an observational study. *Lancet* 2003;**362**:22–9.
2 **Mocroft A**, Katlama C, Johnson A, *et al*. AIDS across Europe, 1994–98: the EuroSIDA study. *Lancet* 2000;**356**:291–6.
3 **Vigilancia Epidemilógica del SIDA en España**. Situación a 30 de junio de 2004. Registro Nacional de casos de SIDA. *Bol Epidemiol Semanal* 2004;**12**:137–40.
4 AIDS epidemic update: 2004. http/thebody.com/unaids/pdfs/Wad2004_report.pdf (Accessed 8 Jan 2007).
5 **Hamers FF**, Downs AM. The changing face of the HIV epidemic in western Europe: what are the implications for public health policies? *Lancet* 2004;**364**:83–94.
6 **Dukers NH**, Spaargaren J, Geskus RB, *et al*. HIV incidence on the increase among homosexual men attending an Amsterdam sexually transmitted disease clinic: using a novel approach for detecting recent infections. *AIDS* 2002;**16**:F19–24.
7 **Katz MH**, Schwarcz MD, Kellogg A, *et al*. Impact of highly active antiretroviral treatment on HIV seroincidence among men who have sex with men: San Francisco. *Am J Public Health* 2002;**92**:388–94.
8 **Del Romero J**, Castilla J, García S, *et al*. Time trend in incidence of HIV seroconversion among homosexual men repeatedly tested in Madrid, 1988–2000. *AIDS* 2001;**15**:1319–21.
9 **Hernández-Aguado I**, Aviñó MJ, Pérez-Hoyos S, *et al*. Human immunodeficiency virus (HIV) infection in parenteral drug users: evolution of the epidemic over 10 years. Valencian Epidemiology and Prevention of HIV Disease Study Group. *Int J Epidemiol* 1999;**28**:335–40.
10 **Alfonso R**, Hurtado I, Espacio A, *et al*. Prácticas de riesgo y seroprevalencia al VIH, VHB y VHC en los pacientes del Centro de Información y Prevención del SIDA de Valencia. *Gac Sanit* 1999;**13**:16–21.

11 **Kim HJ**, Fay MP, Feuer EJ, *et al*. Permutation tests for joinpoint regression with applications to cancer rates. *Stat Med* 2000;**19**:335–51.
12 **National Cancer Institute**. Statistical Research and Applications Branch. http://srab.cancer.gov/software/joinpoint.html (accessed 9 Oct 2006).
13 **de la Fuente L**, Saavedra P, Barrio G, *et al*. Temporal and geographic variations in the characteristics of heroin seized in Spain and their relation with the route of administration. Spanish Group for the Study of the Purity of Seized Drugs. *Drug Alcohol Depend* 1996;**40**:185–94.
14 **de la Fuente L**, Bravo MJ, Barrio G, *et al*. Lessons from the history of the human immunodeficiency virus/acquired immunodeficiency syndrome epidemic among Spanish drug injectors. *Clin Infect Dis* 2003;**37**:S410–15.
15 **Bravo MJ**, Barrio G, de la Fuente L, *et al*. Reasons for selecting an initial route of heroin administration and for subsequent transitions during a severe HIV epidemic. *Addiction* 2003;**98**:749–60.
16 **Castilla J**, de la Fuente L. Trends in the number of human immunodeficiency virus infected persons and AIDS cases in Spain: 1980–1998. *Med Clin* 2000;**115**:85–9.
17 **Alastrué I**, Giner M, Santos C, *et al*. Diagnóstico de la infección por el VIH en atención primaria. *Gac Sanit* 2002;**16**:455.
18 **Agha S**. The impact of a mass media campaign on personal risk perception, perceived self-efficacy and on other behavioural predictors. *AIDS Care* 2003;**15**:749–62.